REMARKS

Claims 21-37 were pending. Claim 32 is canceled without prejudice. Claim 21 is amended. Support for the amendment is found throughout the specification at, inter alia, page 10, lines 5-15. Thus, it is believed that no new matter has been added. Claims 21-31 and 33-37 are pending. No claim is allowed.

Rejection Under 35 U.S.C. § 112, first paragraph - Written Description

Claims 21-37 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement for reasons of record. The Examiner alleges that step (f) of claim 21, oligopeptides that are non-linear, and oligopeptides that are continuous or discontinuous are not supported in the original disclosure. Applicants traverse these rejections.

Applicants respectfully submit that the specification as filed provides adequate written description for the claimed methods. First, the specification provides support for the propagation (or amplification) of the packages containing the polypeptide-encoding nucleotide sequences. For example, the specification states in its discussion of one embodiment of the methods "[after] removal of the non-bound phages by washing, bound phages are eluted from the rods and propagated in bacterial cells." *See* the specification at page 9, lines 12-14. The specification also includes disclosure of isolating nucleotide sequences encoding individual antibodies or peptide after affinity enrichment. *See* the specification at page 10, lines 5-15. Second, the specification adequately describes non-linear oligopeptides. Applicants note that the absence of the specific term "non-linear" fails to render the specification lacking in adequate written description. *See* M.P.E.P. § 2163 (I)(B) (stating that there is no *in haec verba* requirement). The specification discloses other non-linear conformation such as disulfide bridged circular bridge or having peptides that contain more than one disulfide bridge. *See, e.g.*, the specification at page 7, lines 4-10. A person of skill in the art would recognize that a description of a peptide as "linear or compris[ing] another conformation" is a description of a peptide that is linear or non-linear as an alternative way of stating another conformation other than linear is simply to say non-linear. Finally, while Applicants do not agree that the specification fails to provide adequate written description for claim 32, it is canceled herein in an effort to expedite proseuction, rendering the rejection moot.

Applicants further submit that the specification adequately describes the genus of antibodies and antigen binding fragments thereof in sufficient detail to convey to one of skill in the art that Applicants were in possession of the invention at the time of filing. Applicants note that the claimed methods employ antibodies or antigen binding fragments thereof. The specification expressly discloses the use of antibody display libraries using methods known in the art. *See, e.g.,* the specification at page 12, line 1 to page 13, line 9. The use of various types of antibodies or antigen binding fragments is easily achieved using well known methods in the art, and thus does not require extensive description beyond the guidance provided in the specification to fully apprise the skilled artisan regarding the invention. The library of polypeptides is defined as one of antibodies and antigen binding fragments thereof. The specification also provides a working example where a library of synthetic antibodies was constructed using disclosed methods. *See, e.g.,* the specification at page 15, lines 1-15. The examiner seems to be suggesting that specific sequences should be explicitly disclosed because antibodies and their antigen binding fragments are so unpredictable that the skilled artisan cannot readily identify libraries of gene fragments from which to form such libraries. However, the guidance regarding a library of antibodies (or antigen binding fragments) is sufficient for one of ordinary skill in the art. Antibodies are not newly defined in the specification, and identification and manipulation of the appropriate immunoglobulin gene segments to result in such libraries is well known.

The specification expressly discloses the isolation of nucleotides from replicable display packages. *See, e.g.*, the specification at page 10, lines 5-15. It is clear throughout the specification that the disclosed methods can result in the isolation of nucleotide sequences that encode the polypeptides identified as binding particular sequences in its discussion of infection and propagation of the sequences using bacterial cells, use of the genes and nucleotides sequences for subcloning into expression vectors for polypeptide production, and the use of the isolated nucleotide sequences for sequences. Applicants further note that it is the nucleotide sequence in the replicable display packages that permits the transmission and ultimate expression of the encoded antibodies or antigen binding fragments thereof so that the selection process can occur. Therefore, the disclosure in the originally filed specification adequately describes the claimed methods for isolation of particular nucleotides sequences.

In view of the above, Applicants respectfully submit the basis of the rejection may be removed.

Rejection Under 35 U.S.C. § 112, first paragraph - Enablement

Claims 21-37 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking reasonable enablement for reasons of record. According to the Examiner, the specification fails to describe how to readily go about determining an isolated nucleotide encoding any antibodies or fragments thereof that is capable of specific binding to any target antigen. The Examiner also alleges that the specification fails to describe the kind, type, location and length of the overlapping and nonoverlapping oligopeptides from the target protein. The Examiner asserts that the specification fails to describe a derivation of said oligonucleotide from a target protein or a subregion thereof that binds with an antibody of such specificity. Applicants traverse this rejection.

Applicants respectfully submit that the specification provides reasonable enablement for the claimed methods. The Examiner appears concerned about the identification of the appropriate region of the target antigen and the identification of appropriate antibodies for use in the claimed assay is necessary for one of skill in the art to use the claimed methods. However, this is not the case. The claimed methods do not require pre-existing knowledge of either. Using a set of oligopeptides from any region of the antigen, the method permits the identification of an antibody (and its encoding nucleotide sequence) that specifically binds that region. The method does not require knowing anything about a particular epitope or target region of the antigen. Nor does the knowledge of a particular antibody's binding specificity prior to employing it in the assay. Using any type of library of antibodies or antibody binding fragments, the method permits rapid and specific identification of one or more antibodies (or antibody binding fragments) that bind a particular sequence. Because libraries of oligopeptides and antibodies (or antibody binding fragments) can be used simultaneously, the claimed methods avoid the arduous selection process required for hybridoma creation and characterization and eliminate the selection limits associated with immunodominant or antigenic epitopes while expanding the range of novel antibodies available for selection in a rapid and specific manner. In other words, the claimed methods provide a predictable and readily achievable method to identify antibodies that bind a particular region of an

antigen. Further, the expression systems in replicable display packages are well known and readily employed using the guidance and working example provided in the specification. Finally, Applicants are uncertain of the Examiner's position at section 6 on page 10 of the outstanding Action. The claimed method is not directed to the use of an ELISA, but rather to a selection method. Thus, Applicants do not believe that the use of scFv fragments has any relevance to the enablement of the selection method. Additional clarification on this matter would be most helpful.

In view of the above, Applicants respectfully submit the basis of the rejection may be removed.

Rejection Under 35 U.S.C. § 103 (a)

Claims 21-37 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious in view of Burnie et al for reasons of record. Applicants traverse this rejection.

Applicants again submit that Burnie fails to render the claimed methods *prima facie* obvious for reasons of record as well as those discussed herein. Burnie fails to teach each and every element of the claimed methods. For example, Burnie fails to disclose the contacting of a library of antibodies or antigen binding fragments with a library of oligopeptides from an antigen to identify one or more specific antibodies, *i.e.*, step (c). Nothing in Burnie suggests or implies that such a step is desirable or likely to be successful. For this reason as well as those already of record, Burnie fails to render the claimed method obvious.

In view of the above, Applicants respectfully submit the basis of the rejection may be removed.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 313632000600. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 28, 2005

Respectfully submitted,

By _____

Laurie L. Hill, Ph.D.
Registration No.: 51,804
MORRISON & FOERSTER LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
(858) 720-7955